Future of Thrombolytic Therapy - An Indian Context

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Abstract

Acute myocardial infarction has two main treatment modalities in the form of direct angioplasty (PAMI) and intravenous thrombolysis. PAMI is statistically clearly superior to intravenous thrombolysis. However, as ground reality in Indian conditions PAMI remains a distant ideal option for many ST elevation MI patients. In order to bridge the gap between IV thrombolysis and PAMI, early / pre-hospital IV thrombolysis to all and early angiography within 3 to 24 hours is the treatment modality, which needs to be exercised in India. Because of the encouraging results of pharmaco-invasive treatment in acute and long term morbidity and mortality, it should be the prime treatment of management of ST elevation myocardial infarction in India. The future of IV thrombolysis will remarkably be based on whether Indian physicians switch to direct Fibrin Inhibitors like Tenectaplace and Reteplase and whether every patient of ST elevation MI undergoes early angiography or not. If these two changes are accepted for treatment of ST elevation MI, remarkably successful and effective treatment could be offered in a place like India, which is too vast and too diversioned and too socio-economically irrelevant for the ideal treatment of PAMI. In conclusion, early / pre-hospital thrombolysis with Tenectaplace / Reteplase and angiography within 3 to 24 hours is the way to go in future in India.

Advantages of IV Thrombolysis (Indian Context)

1. Easy availability.
2. Less expertise required.
4. Ease of administration (peripheral venous line).
5. Acceptable complication rates.
6. More than 75% infarction-related arteries would be patent when taken on cath table.
7. Hemodynamically and electrically stable patient for PCI.
8. Well-defined lesions rather than total occlusions.

Ideal Adjuvant Protocol for IV Thrombolysis

a. S/L nitrate, sedation, O₂.
b. Soluble Aspirin 325mg, Clopidogrel 300mg.
c. Weight-adjusted TNK or Reteplase or STK.
d. High dose Atorvastatin, Ramipril.
e. Betablockers as indicated.
f. Avoid Nikorandil, Trimetazidine, Ranolazine, Ivabradine.
g. Enoxaparin or Raviparin SC for 7 days.

Failed IV Thrombolysis

Diagnosis : (After 90 min to 2 hrs of completion of IV thrombolysis).
1. Persistent chest pain.
2. New onset heart failure.
3. Non resolution of ST segments.
4. Hemodynamic instability.
5. Electrical instability.

Treatment

1. Intervention of culprit artery at least at the earliest.

Future of acute myocardial infarction management in India is in “Early thrombolysis to all and early angiography (3 to 24 hours) in all” ST elevation MI (STEMI) patients – with or without successful thrombolysis.

After a ginger start in early eighties, thrombolysis with STK reached nooks and corners of India. Urokinase shared “not a small” percentage. In the last 3 years TNK and reteplase have made an appearance. The future of thrombolysis in India rests in these two agents, especially TNK.

Primary angioplasty in acute myocardial infarction (PAMI) is proven the world over as the gold standard of treatment by way of establishing high percentage of reperfusion and complete reperfusion (TIMI III, good TMP and TFC score). But this treatment modality is available to less than 10% STEMI in India as of today. In USA, 28% of STEMI get PAMI and this percentage is higher in European countries with good transfer facilities.

In Indian conditions, even small towns have population above 1,00,000. Traffic congestions and transfer to hospitals take a long time. Initial delay is by the patient due to lack of awareness. Next delay is due to lack of transfer facilities. (In small towns where reaching a hospital quickly is possible, hospital with PAMI capabilities are not available). The third delay is at tertiary care hospital where reaching from casualty to establishing TIMI III flow has its own delay of formalities, finances, round the clock man power and availability of cath lab in busy hours. All these situations are expected to get worse in India in the future!

Public awareness can be increased about early detection (symptoms) of AMI, early treatment, golden hour and recognising AMI. Physician-based smaller hospital whether in villages, smaller towns or suburbs of cities will play a crucial role.

Such hospitals should thrombolyse these patients on first contact with agents like TNK (easy administration, no anaphylactic reactions, no infusions). The relatives and patient then get a breathing period of moving to a cath lab facility in next 24 hours. The breathing space allows them to choose the doctor of their choice, arrange finances, gather manpower, complete insurance formalities (All very important in Indian context). In addition, this breathing period has not done the myocardium any harm, due to early thrombolysis and recanalised culprit artery.

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2. Abciximab preferred agent for PCI in this subset.
3. IV Eptifibatide (strictly 2 hrs after completion of IV thrombolysis) for those who are not undergoing PCI.

**Some Grey Zones of IV Thrombolysis**

a. Within first hour of chest pain, IV thrombolysis results could be on par with PCI.
b. STK, UK, TNK, Reteplase will recanalise equal number of culprit arteries at the end of 24 hours but within first hour of completion of treatment, fibrin-specific agents are more effective. Because time is muscle in STEMI, benefit to the myocardium and long term outcome favours use of TNK and Reteplase.
c. Chest pain does not mean pain of infarction. Initially many hours could be pain of critical ischemia; therefore, if a patient presents with ongoing chest pain, ST elevation and especially reciprocal ST changes, he should be considered for IV thrombolysis despite apparently long hours of chest pain.
d. Half life of IV thrombolysis varies from 17 minutes to 45 minutes. Considering additional use of adjuvant anticoagulants, intervention should be delayed for atleast 3 hours after completion of IV thrombolytic treatment, in order to avoid bleeding complication during PCI. If earlier interventions are required, radial route interventions should be preferred.
e. Recanalization of infarction related artery in first 6 hours saves myocardium, beyond 6 hours “open artery” is aimed at, rather than salvage of myocardium. Beyond 6 hours of true infarction process, IV thrombolysis becomes highly ineffective.

**Future of Thrombolysis – In India can be Visualised as**

1. First on contact competent medical person (consultant physician in most cases) should plan thrombolysis in all except obvious PAMI cases.
   - Door to TIMI III flow time less than 90 min, in STEMI with more than one hour chest pain
   - Cardiogenic shock.
2. For all cases eligible for thrombolysis, correct adjuvant protocol should be standardized (contraindications of thrombolysis ruled out).
3. Most cases should be thrombolysed with fibrin-specific agents. (Use of GPIIb3A inhibitors should be discouraged as primary agents in STEMI).
4. All cases should be subjected to coronary angiography in 3 to 24 hours.
5. By government policies, insurances and awareness, no patient should be deprived of correct treatment for financial reasons.
6. One toll free number for all cities and towns for call of cardiac ambulance, capable of tele-transfer of ECG and IV thrombolysis with TNK.

By this kind of approach, culprit artery recanalization would be achieved in nearly 75% of all STEMI. This will lead to preservation of myocardium, better LVEF, less heart failure, death and improved prognosis and above all, less health care costs.

For those who do not have significant residual lesions can be rehabilitated faster. Those who deserve angioplasty will undergo it with stable hemodynamics, good TIMI flows on arrival to cath lab. Less gadgets and drugs (IAPB, Abciximab) get used in stable patients during procedure, leading to less expensive procedure. Also, most such procedures will be done during working hours, which has its own advantage. Finally those who require surgery can be sent for surgery after appropriate delay.

All of us treat very young patients of STEMI. The predominant pathology in the coronary in such cases is thrombus rather than traditional atherosclerotic plaques. Such individuals if treated early with effective thrombolysis, can have practically normal coronaries. In future for this special Indian subset, every attempt should be made for early thrombolysis because that could be the only therapy required for these young individuals and unnecessary stenting would get avoided.

For a vast country like India, where infrastructure is not developing with the speed of population, thrombolysis is the treatment of choice. With advent of more efficient thrombolytic agents, one should not hesitate to thrombolise. First contact (small nursing homes, satellite hospitals, casualty of corporate hospitals) should be “pre hospital” areas of thrombolysis. This will reduce the loss of myocardium and reduce health costs.

“Early thrombolysis to all and early angiography to all” should be the future of managing STEMI in Indian context. Thus STEMI can be a comforting hot cup of “TEA” (Thrombolysis - Early Angiography) for Indian patients ‘in Future!’